



Heterologous Production of Polyketides in Fungi

Mølgaard, Louise; Hansen, Bjarne Gram; Mortensen, Uffe Hasbro; Patil, Kiran Raosaheb

Publication date:
2009

Document Version
Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

Citation (APA):
Mølgaard, L., Hansen, B. G., Mortensen, U. H., & Patil, K. R. (2009). *Heterologous Production of Polyketides in Fungi*. Poster session presented at 1st Systems Biology as a driver for Industrial Biotechnology Workshop, Istanbul, Turkey. <http://www.sysbio.se/SYSINBIO/index.html>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Heterologous Production of Polyketides in Fungi

Louise Mølgaard, Bjarne G. Hansen, Uffe H. Mortensen and Kiran R. Patil

Polyketides are the source of some of the most potent antibiotics and anticancer agents available today. They constitute a large group of natural compounds, produced primarily by fungi and bacteria. However, the productivity is often very low in the native producer. Thus, expression of polyketide gene clusters in an industrially relevant microorganism presents a great potential. Towards fulfilling this potential we are working with the three fungal species, viz. *S. cerevisiae*, *A. niger* and *A. nidulans*, which are all well suited as hosts for polyketide production. The overall goal of the project is to construct microbial super hosts through the use of state of the art genetic engineering and *in silico* modeling tools.

Polyketides belong to one of nature's most diversified groups of compounds. Among the polyketides can be named the cholesterol lowering agent lovastatin and the antibiotic erythromycin. We are studying two polyketides: mycophenolic acid (MPA) which is used as an immunosuppressant and 6-methylsalicylic acid (6-MSA) that has antibiotic properties. By studying three different species capable of producing heterologously expressed polyketides, we aim at designing more efficient polyketide cell factories that will work in a plug-and-play fashion. The overall strategy towards achieving this goal is illustrated in figure 1.

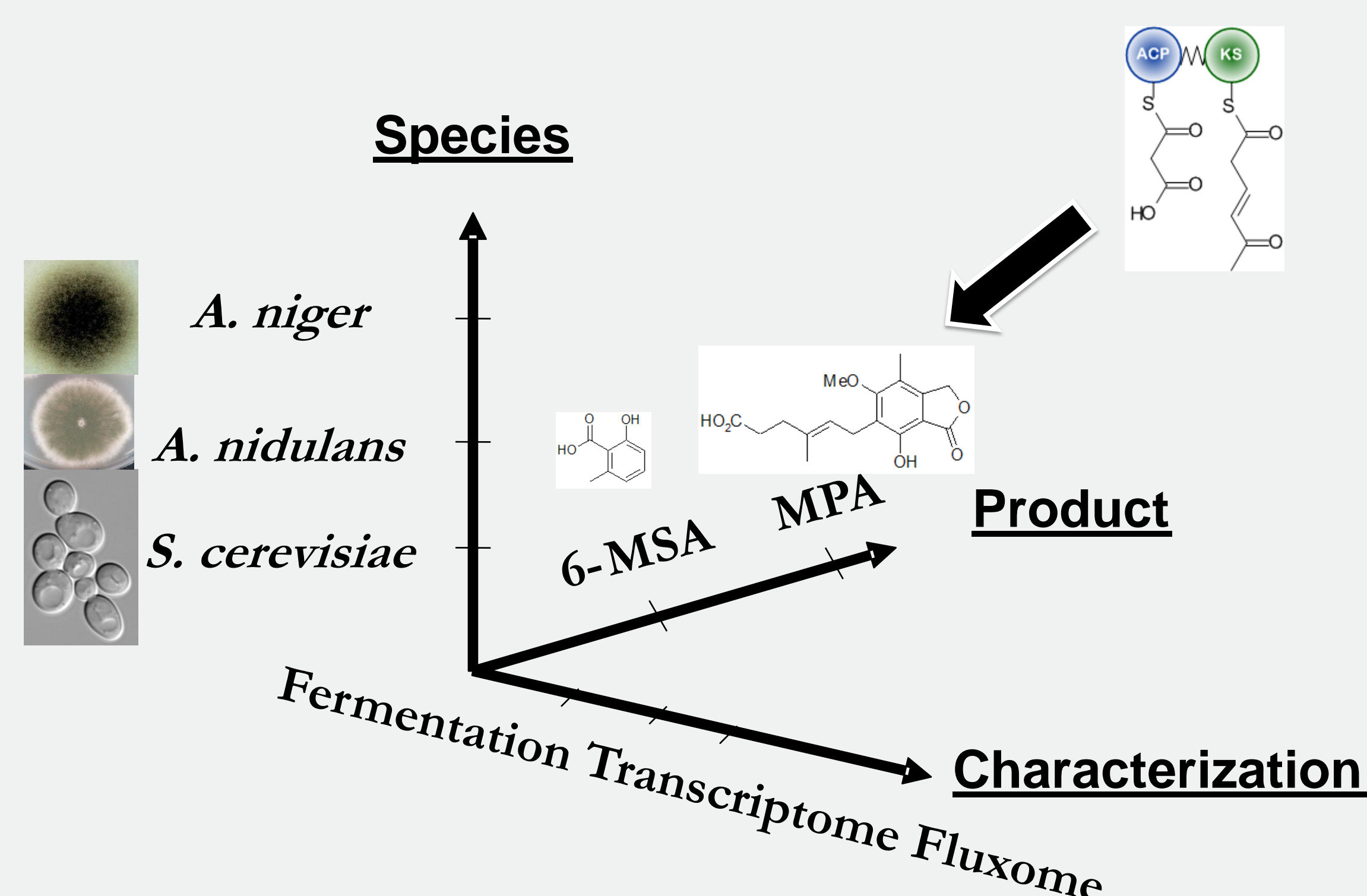


Fig. 1 Overall strategy for the construction of polyketide cell factories.

Targeted Integration of the 6-MSA PKS in *A. nidulans*

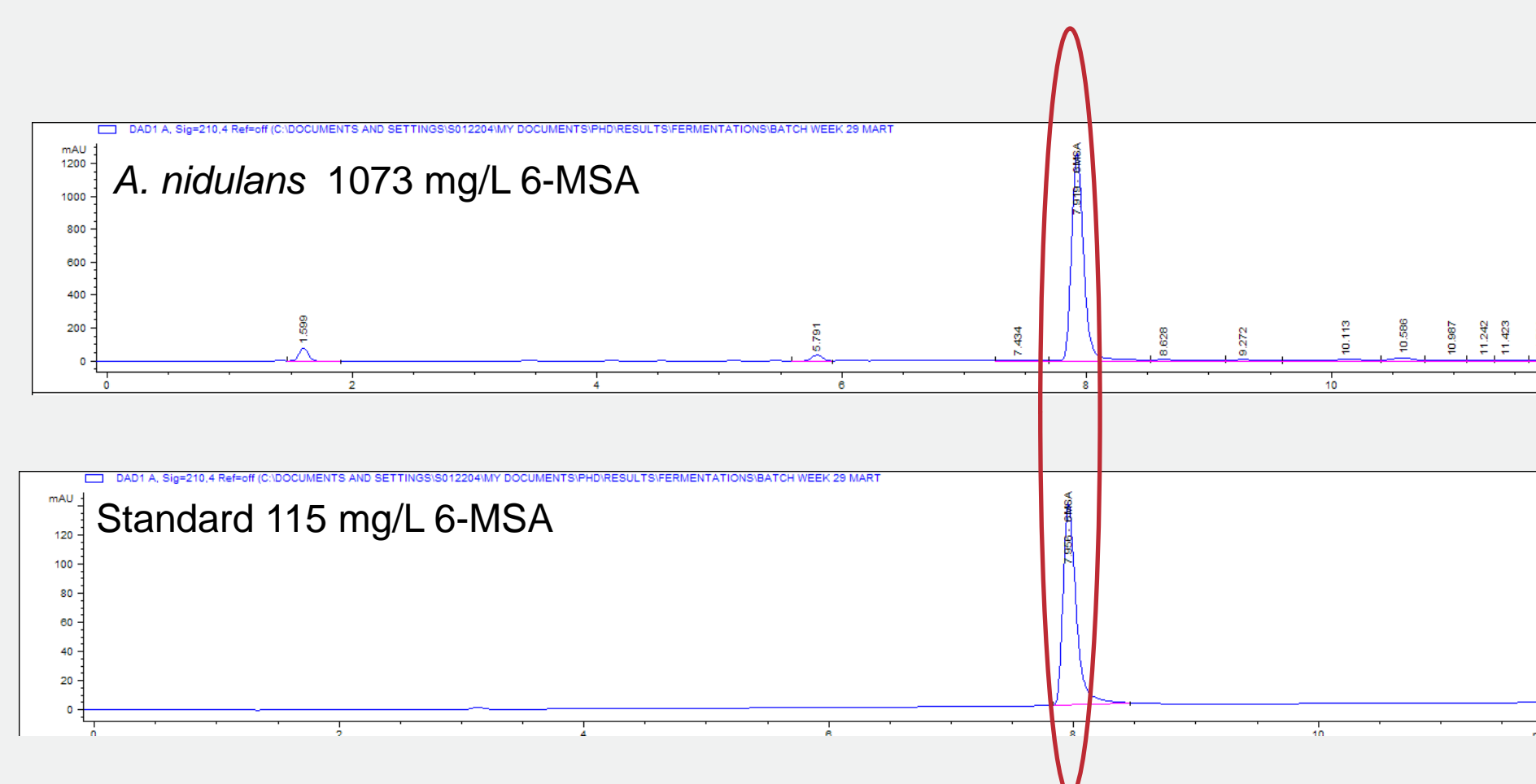
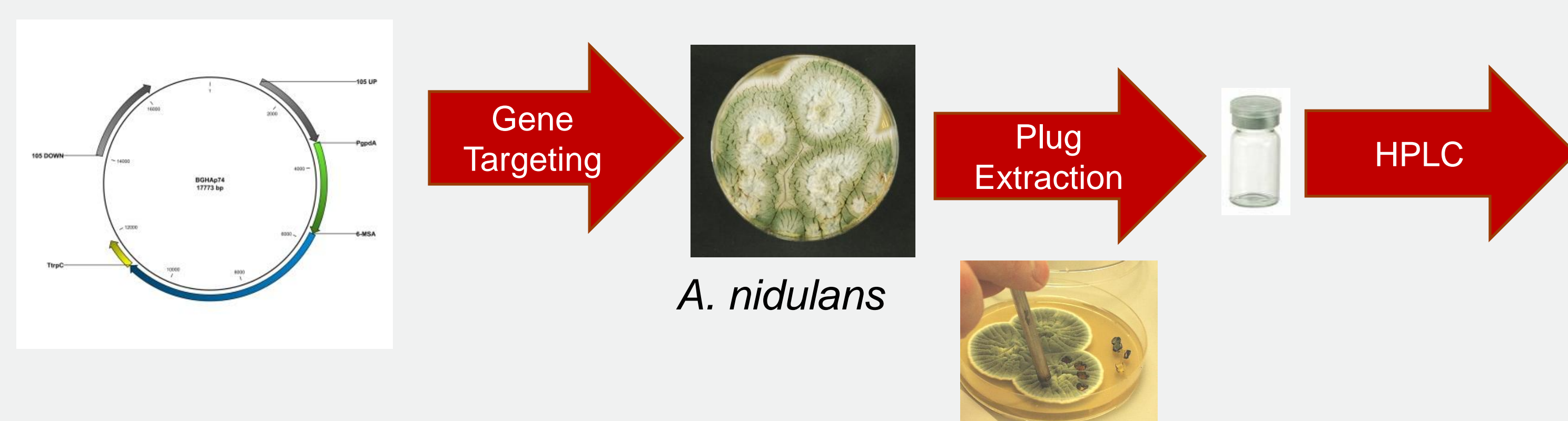


Fig. 2 6-MSA production in *A. nidulans* after targeted integration of the 6-MSA synthase.

Targeted Integration of the 6-MSA PKS and *npaA* PPTase in *S. cerevisiae*

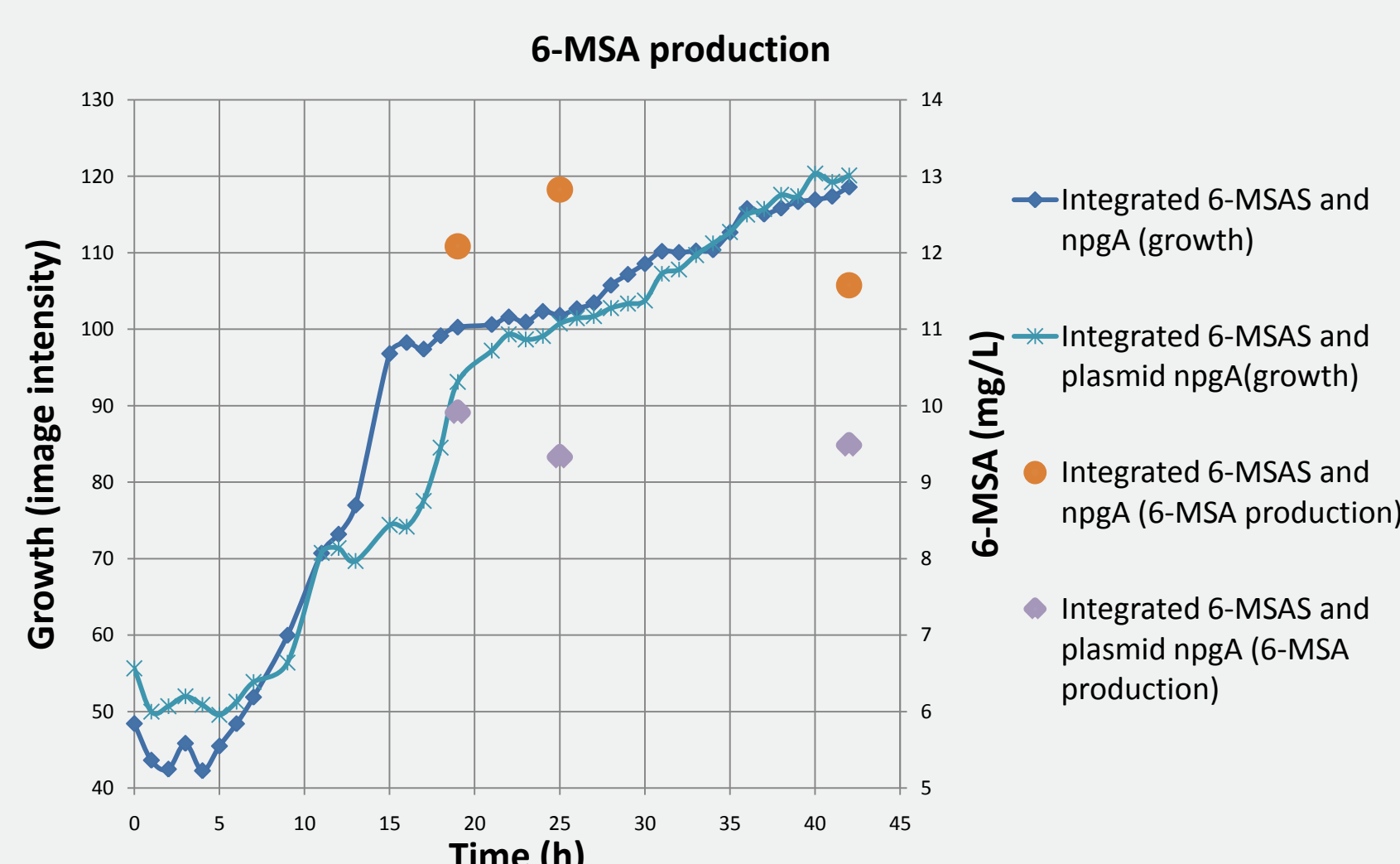
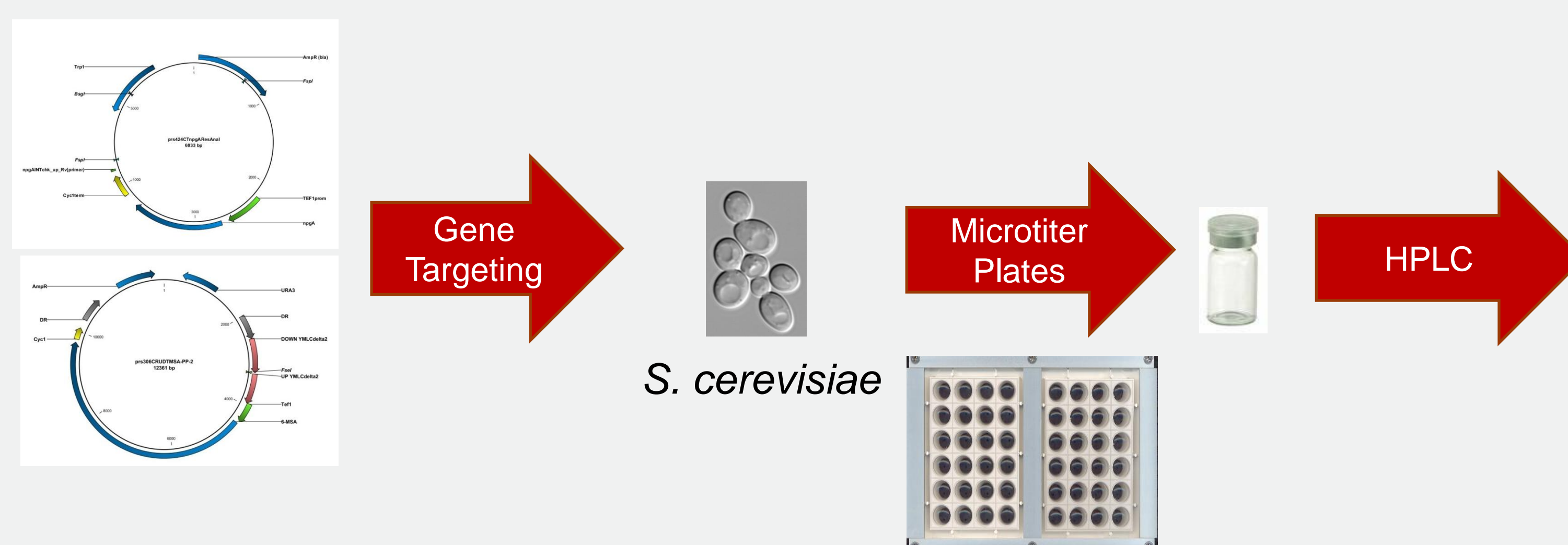


Fig. 3 6-MSA production in *S. cerevisiae* using a high throughput microtiter platform after targeted integration of the 6-MSAS and the *npaA* PPTase. The strain was compared with a strain that only has the 6-MSAS integrated and the PPTase on a multicopy plasmid. As having only one copy of the PPTase did not decrease 6-MSA production, it is clear that the polyketide synthase expression is the limiting factor in polyketide production.

The stable heterologous production of polyketides in *S. cerevisiae* and *A. nidulans* presents the first step in the construction of efficient cell factories. Polyketide synthases are proving to be the source of several new medically relevant compounds. Having a polyketide cell factory platform will therefore be a significant step towards economic and sustainable production of this important class of natural products.